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Current Outlook for ^{99m}Tc Distribution Based on Electron Accelerator Production

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CURRENT OUTLOOK FOR ^{99m}Tc DISTRIBUTION BASED ON ELECTRON ACCELERATOR PRODUCTION

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Update of a previous study by
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ABSTRACT

In 1999 a practical example illustrating the economical and reliable production of ^{99m}Tc from an accelerator was developed. It included the realistic costs involved in establishing and operating the accelerator facility and the distribution of the ^{99m}Tc to regions in Florida. However, the technology was never commercialized.

Recent political and economic developments prompted this second look at accelerator produced ^{99m}Tc. The practicality of this system in 2007 dollars was established to account for inflation and current demand. The same distribution model and production schedule from the Global '99 study were used. Numbers were found using current rates and costs where possible and indexed estimations when necessary.

Though several of the costs increased significantly and the sale price remains at approximately 35¢/mCi, the unit cost of ^{99m}Tc throughput only increased from 12.8¢/mCi to 25.0¢/mCi or approximately double from 1999 to 2007 thus continuing to be economically viable. This study provides ground work for creating business development models at additional locations within the U.S.

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I. INTRODUCTION

The initial studies, hereafter referred to as Initial studies, of an accelerator-based ^{99m}Tc supply have assessed product quality and price based on thermal separation units (termed 'goats' compared to current chemical separation units termed cows) that are located with the accelerator.[2,3,4] However, the losses and inefficiencies associated with the distribution of the intermediate ^{99}Mo product were not fully captured. The Global '99 study[1] more fully evaluated these effects in a realistic distribution scenario based on 1996 cost and demand estimates. The scope of the Global '99 study included (1) selecting an updated suitable target market area, (2) making choices about the throughput and location of the accelerator, (3) making related choices about the number and location of regional nuclear pharmacies, as well as the number of goats to be deployed at each, (4) evaluating and making changes, where feasible, to the system design (especially the goats) to afford a more efficient system and (5) evaluating the overall product cost to determine the impact of realistic distribution. The present study (1) utilizes the Global '99 methods to appropriately fit current demand, (2) considers potential system design changes to the previous Global '99 method, (3) compares costs and demand, and (4) demonstrates that the system established in 1999 is still practical. The majority of the Global '99 study has been presented here for background and informational purposes.

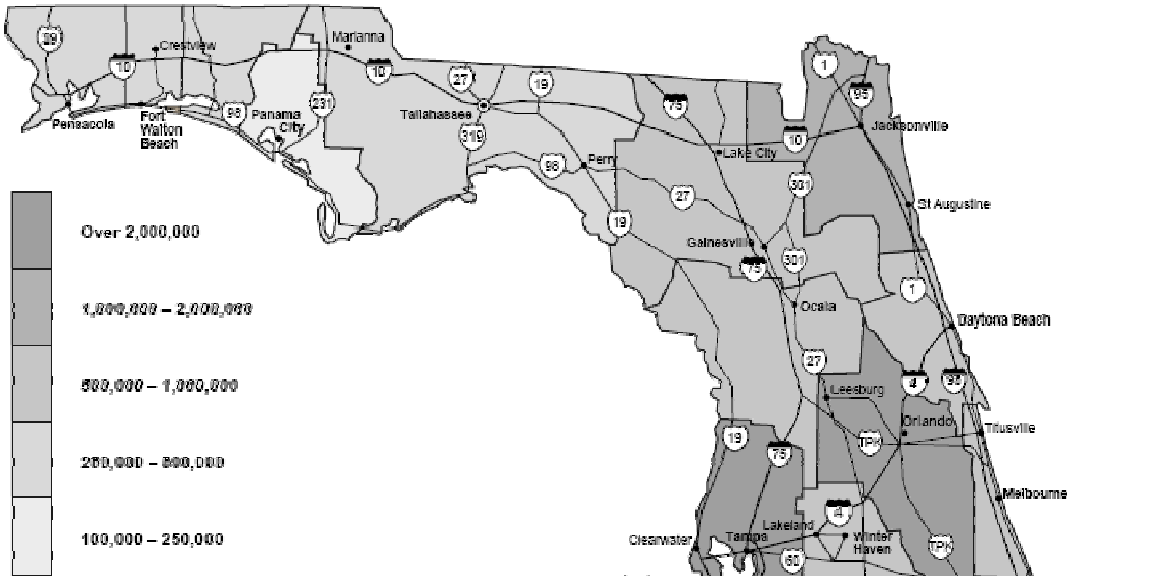
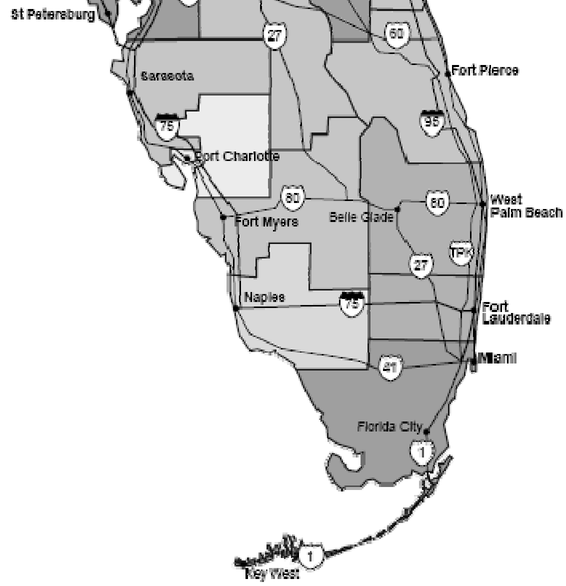

Fig. 1. 'Adjusted' Florida Metropolitan Statistical Areas.

II. SELECTION OF THE STUDY AREA

The Initial studies at the INL have established that a single accelerator will be able to supply about 1500-2000 doses of ^{99m}Tc per day. The entire U.S. population of 302 million people, a 14% increase over 1996, uses about 14.6 million doses per year or about 46,800 doses per weekday compared to 38,500 doses per weekday in 1996, a 22% increase in demand.[5] (The demand drops to about 50% on weekends.) This leads to the claim of the Initial work that about two dozen accelerators could supply the U.S. demand. On a per capita basis, about 155 doses are needed per weekday per million people. Thus, a single accelerator might be expected to serve a population of somewhat more than 13 million people.

With a population of nearly 18 million, a 20% increase from 1996, and a land area of 55,000 square miles, Florida was chosen for the Global '99 study since it is representative of a populous yet dispersed customer base. With a little over 5% of the U.S. population, Florida needs about 2870 doses, compared to 2088 doses in 1996, of ^{99m}Tc each weekday (and only about half of this on weekends). Using Global '99 methods, only a portion would be served without dramatic changes to the process, therefore for this study it is assumed only the 2088 daily doses from the Global '99 study were sold. This represents about a 73% share of the 2007 market demand in Florida.

III. POPULATION DEMOGRAPHICS AND CURRENT ^{99m}Tc SUPPLY FOR FLORIDA

This study is based on 2005 U.S. Census estimates from the 2000 census update. Further, the population is growing at about 1.2% per year in Florida, bringing the 2007 estimated total to 18.3 million. While there are 67 counties and 20 metropolitan statistical areas (MSAs) in Florida, the 33 least populated counties are not included in any MSA. The 2007 MSA population totaled 16.8 million, while the entire state totaled 18.3 million. i.e., about 8.2% of the population lives in the 33 rural counties outside of the MSAs.

Table 1. Baseline Melt-Technology Goat Milking Schedule.

EOB Time of Day	Length of Irradiation	Mo-99 at EOB	Tc-99m at EOB
2 a.m.	23 hr	26.18 Ci	15.528 Ci

Separation Efficiency	92%
Wash Efficiency	92%
Overall Efficiency	85%
Evaporative Loss	3%
Usage Efficiency	70%

Milking	Milking Time of Day (a.m.)	Time after EOB (hr)	Mo-99 in Goat (Ci)	Tc-99m in Goat (Ci)	Tc-99m Milked (Ci)	# Doses 6 hours later	Cumulative Doses	Day or Goat #
	8	6	24.580	19.011	16.159	282.8		
1	8	6	23.820	1.484				
	2	24	19.714	16.568	14.082	246.4		
2	2	24	19.085	1.293				
	5	27	18.492	5.803	4.933	86.3	615.6	1
3	5	27	17.883	0.453				
	8	30	17.327	4.901	4.166	72.9		
4	8	30	16.737	0.383				
	2	48	13.852	11.558	9.825	171.9		
5	2	48	13.363	0.902				
	5	51	12.948	4.061	3.452	60.4	305.2	2
6	5	51	12.474	0.317				
	8	54	12.087	3.420	2.907	50.9		
7	8	54	11.628	0.267				
	2	72	9.624	8.031	6.826	119.5		
8	2	72	9.244	0.627				
	5	75	8.957	2.811	2.390	41.8	212.1	3
9	5	75	8.589	0.219				
	8	78	8.322	2.355	2.002	35.0		
10	8	78	7.965	0.184				
	2	96	6.592	5.501	4.676	81.8		
11	2	96	6.297	0.429				
	5	99	6.102	1.917	1.629	28.5	145.4	4
12	5	99	5.816	0.150				
	8	102	5.635	1.596	1.356	23.7		
13	8	102	5.358	1.125				
	2	120	4.434	3.701	3.145	55.0		
14	2	120	4.205	0.289				
	5	123	4.075	1.281	1.089	19.1	97.8	5
15	5	123	3.852	0.100				

Total Tc-99m Milked	Total Doses
78.6 Ci	1376

Note: An Average Tc-99m dose is 20 mCi at administration.

A. 'Adjusted' Metropolitan Statistical Areas (MSAs)

One issue the Global '99 study addressed was the assignment of the 8.2% of the population living outside MSAs into logical choices of where they would obtain diagnostic medical imaging radioisotopes. Case-by-case, each of the 33 counties was evaluated to determine which metropolitan areas would likely supply the residents with unit doses of ^{99m}Tc. In this way, 'adjusted MSAs' were defined that properly capture the entire 18.3 million 2007 population of Florida. The adjusted MSAs are shown in Figure 1. Then, the region desirable for distribution by a single accelerator was selected. It was determined that a population of about 13.3 million could adequately be served by the single accelerator as will be seen later in this study. Therefore, this study assumes production of ^{99m}Tc at full capacity of the accelerator and a 72.8% share of the Florida market. Growth is possible as processing and distribution is optimized.

B. Current ^{99m}Tc Supply in Florida

Prorated by the above per capita dose rate, the selected region and percentage of Florida's population requires 2088 doses per weekday. The supply of ^{99m}Tc in the U.S. is now principally supplied by about 382 regional nuclear pharmacies nationwide. This represents a 255% increase over the 150 regional nuclear pharmacies in 1999. Thirty-seven of these pharmacies are located in Florida compared to 11 in 1999. The regional areas of Miami and Tampa have head-to-head competition. If we lump competing centers together, this means that Florida is effectively served from 7 regional centers today. It was assumed that the current distribution of ^{99m}Tc doses is fully served by these centers alone. For any subsequent business development studies, it may be noted that each 'adjusted MSA' has an independent nuclear pharmacy. Over the state, the average delivery distance by car of a unit dose of ^{99m}Tc to a hospital or clinic from a nuclear pharmacy is only about 17 miles.

IV. OPTIONS TO ACHIEVE DESIRED ACCELERATOR ^{99}Mo THROUGHPUT

To understand the modifications to the single accelerator and collocated separation system required to meet a 2088 dose/day demand in the Florida region with the given market share, it begins with the melt-technology[6] baseline system from the initial cost estimate study.[2] A spreadsheet analysis of the overall irradiation and separation performance is found in Table 1. Using a 14.4g ^{100}Mo target and a 14 kW, 40 MeV electron accelerator, a total of 26.2 Ci of ^{99}Mo is induced in 23 hours at the end of bombardment (EOB) at 2 a.m. each day. The target is to be dissolved in nitric acid, loaded into a single goat and available for the first separation six hours later, at 8 a.m. A herd of five goats performed all of the separations, three times a day. The complete milking schedule is shown for the 15 milkings of one goat. For each milking, two lines appear, showing the same time of day. The first line shows conditions just prior to milking, and the second just after. Since a new goat is loaded each day on the same schedule, the 5 day milking schedule is, in fact, equivalent to the five goats in the herd on any given day if the word 'Day' is switched to 'Goat Number'. This schedule is based on the melt-technology goats, which were conservatively assumed to have an overall efficiency of 85% and MoO_3 evaporative losses of 3% per milking cycle. The initial cost estimate study baseline system would produce a total of 1376 doses at time of sale each weekday. The sensitivity of the throughput to the percent evaporative loss per cycle is shown in Figure 2 of the Global '99 study, where each percent increase in evaporative loss per cycle equates to a 5% increase in required throughput.

The authors of the Global '99 study had two objectives in the modifying of the system. First, the required 1996 demand of 2088 doses had to be met. Second, the problems caused by separating smaller samples coming from the use of a much larger number of goats (placed at the selected regional pharmacy sites) had to be anticipated. The central difficulty with melt-technology is the evaporative loss, which does not scale down with smaller separation size—the loss is fixed by the goat condenser dimensions and is unrelated to the charge of ^{99}Mo loaded in the goat. With this in mind, the authors decided to explore the viability of the alternative powder-technology[7] goats. This technology does not suffer from evaporative losses and has had limited demonstration of improved separation efficiency. However, the technology does require a more time consuming redissolve/reprecipitate step between milkings in their operation.

A. Powder Technology for ^{99m}Tc Separation in Goats

The Global '99 baseline powder-technology separation schedule is shown in Table 2. The same initial loading of ^{99}Mo is made available as in the melt-technology case. With the elimination of evaporative losses and slightly higher efficiencies of separation and washout, the doses at time of sale were improved to 1720, still short of the 2088 goal. The sensitivity of the throughput to the thermal separation or washout efficiency is shown in Figure 3 of the Global '99 study, where each percent increase in efficiency equates to about a 1% decrease in required throughput. The sensitivity to washout efficiency is about half again as large as the sensitivity to thermal separation efficiency. For the goal quantity to be met, the EOB ^{99}Mo must be increased to 31.8 Ci, up 21.4% from 26.2 Ci. Further efficiency improvements cannot meet this need. Rather, from the original baseline study it was determined that a target almost exactly double in size (28.9 g) under the same accelerator beam would meet this required throughput. Additional options for increasing the ^{99}Mo production are described in Section IV.D.

B. Location of the Accelerator and the Regional Pharmacies

Increasing the ^{99}Mo throughput by doubling target size only partly meets the objective since it was still based on the initial cost estimate study's[2] set of five centralized goats for the separation. From the Global '99 demographics, the authors concluded that Florida might be served by as few as seven regional nuclear pharmacies,

Table 2. Baseline Powder-Technology Goat Milking Schedule.

EOB Time of Day	Length of Irradiation	Mo-99 at EOB	Tc-99m at EOB
2 a.m.	23 hr	26.18 Ci	15.528 Ci

Separation Efficiency	98%
Wash Efficiency	95%
Overall Efficiency	93%
Evaporative Loss	0%
Usage Efficiency	70%

Milking	Milking Time of Day (a.m.)	Time after EOB (hr)	Mo-99 in Goat (Ci)	Tc-99m in Goat (Ci)	Tc-99m Milked (Ci)	# Doses 6 hours later	Cumulative Doses	Day or Goat #
	8	6	24.580	19.011	17.699	309.7		
1	8	6	24.580	0.380				
	2	24	20.343	16.952	15.782	276.2		
2	2	24	20.343	0.339				
	5	27	19.711	5.451	5.075	88.8	674.7	1
3	5	27	19.711	0.109				
	8	30	19.100	5.126	4.773	83.5		
4	8	30	19.100	0.103				
	2	48	15.807	13.148	12.241	214.2		
5	2	48	15.807	0.263				
	5	51	15.317	4.235	3.943	69.0	366.7	2
6	5	51	15.317	0.085				
	8	54	14.841	3.983	3.709	64.9		
7	8	54	14.841	0.080				
	2	72	12.283	10.217	9.512	166.5		
8	2	72	12.283	0.204				
	5	75	11.902	3.291	3.064	53.6	285.0	3
9	5	75	11.902	0.066				
	8	78	11.532	3.095	2.882	50.4		
10	8	78	11.532	0.062				
	2	96	9.544	7.939	7.391	129.3		
11	2	96	9.544	0.159				
	5	99	9.248	2.557	2.381	41.7	221.4	4
12	5	99	9.248	0.051				
	8	102	8.961	2.405	2.239	39.2		
13	8	102	8.961	0.048				
	2	120	7.416	6.169	5.743	100.5		
14	2	120	7.416	0.123				
	5	123	7.186	1.987	1.850	32.4	172.1	5
15	5	123	7.186	0.040				
					Total Tc-99m Milked		**Total Doses**	
					98.3 Ci		1720	

Note: An Average Tc-99m dose is 20 mCi at administration.

compared to effectively 11 pharmacies then. This study shows that 2007 Florida demographics could also be served by seven regional pharmacies. The proposed 2007 supply network is detailed in Table 3 and shown in Figure 2. The heavy infrastructure of air travel in the Orlando area can be exploited by placing the accelerator near the Orlando airport. A nuclear pharmacy is also located in Orlando, although it does not need to be near the airport. Tampa is another pharmacy location; it can easily be served from the accelerator by ground transportation, being only about 90 miles away. The other five pharmacies are at West Palm Beach, Jacksonville, Miami, Pensacola, and Ft. Myers, which are all served by air. If commercial air is not prohibitive, commercial passenger jet service is available from Orlando with departures scheduled between 7 and 8 p.m. daily to every one of these cities. In each case the flying time is about one hour, so the ^{99}Mo deliveries would arrive at the pharmacies at

Table 3. Accelerator-Based Tc-99m Distribution for Florida with 7 Regional Nuclear Pharmacies.

(Boldface entries are regional nuclear pharmacy locations.)

Adjusted MSA Grouping	2007 Population	MSA Doses/Day*	Served by Pharmacy	Distance (miles)	Pharmacy Doses/Day*	72.8% of Market
Orlando, FL MSA	2,018,599	314	1	10	596	434
Lakeland-Winter Haven	670,807	105	1	47		
Melbourne-Titusville-Palm Bay, FL MSA	543,444	85	1	54		
Deltona-Daytona Beach-Ormond Beach, FL MSA	589,514	92	1	71		
West Palm Beach-Boca Raton, FL MSA	1,295,672	202	2	10	574	418
Ft. Lauderdale, FL MSA	1,818,026	283	2	43		
Fort Pierce-Port St. Lucie, FL MSA	572,189	89	2	54		
Tampa-St. Petersburg-Clearwater, FL MSA	2,743,594	427	3	71	540	393
Sarasota-Bradenton-Venice, FL MSA	723,551	113	3	53		
Jacksonville, FL MSA	1,299,726	202	4	10	444	324
Gainesville, FL MSA	513,610	80	4	62		
Ocala, FL MSA	571,730	89	4	95		
Tallahassee, FL MSA	464,060	73	4	163		
Miami, FL MSA	2,519,054	392	5	10	392	285
Pensacola, FL MSA	447,468	70	7	10	142	103
Panama City, FL MSA	203,674	32	7	103		
Fort Walton Beach, FL MSA	256,128	40	7	40		
Fort Myers - Cape Coral, FL MSA	633,625	99	6	10	179	131
Punta Gorda, FL MSA	192,980	30	6	34		
Naples, FL MSA	319,999	50	6	35		
Total Florida	**18,397,450**	**2867**		**37 (avg.)**	**2867**	**2088**

*Basis of Estimate:

14,600,000 Doses per Year for the 302,000,000 U.S. Population 52 x 6 =312 'Full' production days per year (Sat-Sun fall to 50%)

10-11 p.m., allowing an hour or two to accomplish pickup and ground travel to the pharmacy. The necessary number of doses dispensed by each pharmacy is listed in Figure 2, along with the proposed supply lines to the adjacent MSAs. Note that the average distance of delivery of a dose of ^{99m}Tc by car from this smaller set of seven pharmacies rises to about 37 miles, which is felt to be a manageable increase from the approximate 17 mile average.

C. Shipment of ^{99}Mo Target Material to the Regional Pharmacies

Deploying the ^{99m}Tc supply with seven regional pharmacies implies that a herd of goats will reside at each pharmacy. With the same five-day milking schedule, this means that five goats will be active in each pharmacy, for a total of 35 goats altogether. Two options for supplying ^{99}Mo to them were examined by the Global '99 study. First, the accelerator targets could be adjusted to the appropriate size to meet the individual pharmacy needs. At EOB the target is simply disassembled and packed for shipment as activated Mo metal discs. To meet the first 7 p.m. flight, the EOB would need to be scheduled for no later than 6 p.m.

The second option was to dissolve and oxidize the target in nitric acid, evaporate it to dryness, and redissolve the precipitate MoO_3 in NH_4OH. This was previously studied in some detail with supporting experiments to demonstrate the proposed kinetics.[8] The unit operations are summarized in Table 4. The key result was that centralized preparation of aliquots will require only 3 hours. This has the especially nice advantage that ^{99}Mo

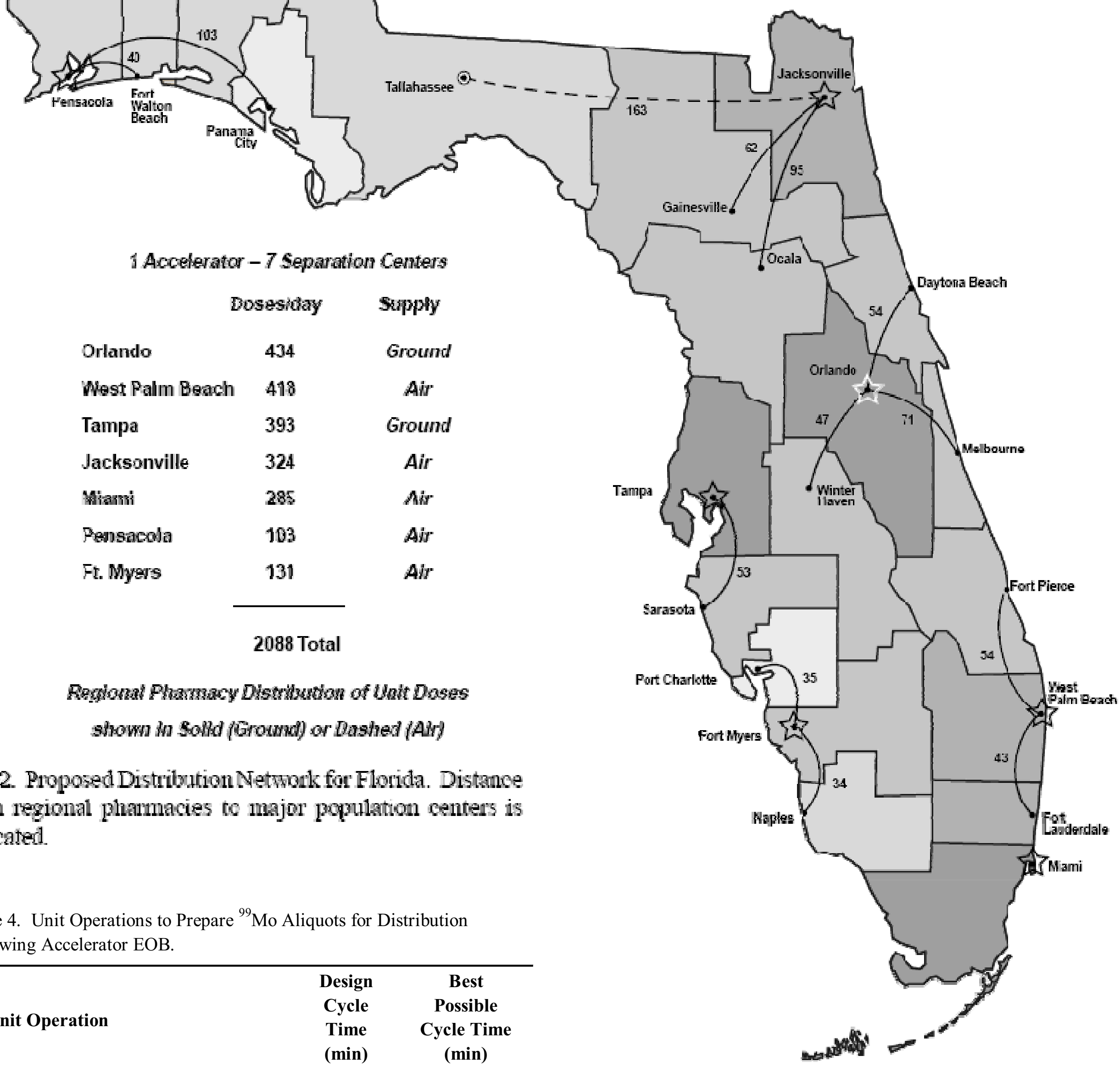

Fig. 2. Proposed Distribution Network for Florida. Distance from regional pharmacies to major population centers is indicated.

Table 4. Unit Operations to Prepare ^{99}Mo Aliquots for Distribution Following Accelerator EOB.

Unit Operation	**Design Cycle Time (min)**	**Best Possible Cycle Time (min)**
1. Transfer targets from accelerator	15	10
2. Dissolve pellets in 7 *M* HNO_3	75	70
3. Evaporate nitritc acid to dryness	75	60
4. Add 7 *N* NH_4OH to dissolve residue	10	10
5. Dispense aliquots for shipping	20	15
Total Cycle Time	**195** (3hr 15 min)	**165** (2hr 45 min)

dispensed and shipped as small aliquots greatly facilitates alteration of the amount delivered to each pharmacy. This flexibility even allows the possibility of 'load following' the actual bookings of next day prescriptions at the pharmacies. To meet the first 7 p.m. flight, the EOB would need to be scheduled for no later than 3 p.m. The sensitivity of the required throughput to the time delay from EOB until first separation (at 2 a.m.) is shown in Figure 5 of the Global '99 study. Each additional hour's delay causes a fairly modest 1% increase in required system throughput, so the distributed system is not overly sensitive to the time required for target processing before distribution.

D. Adjusting the Accelerator Option

The Global '99 study allowed only the options listed above for increasing throughput of the ^{99}Mo. However, adjusting the power level of the accelerator would also allow the adjustment of the supply. A 19.5 kW, 40 MeV electron accelerator would be able to provide the full demand of doses/day for Florida. The second option is to operate two smaller regional accelerators of about 10 kW power level each. Alternatively, increasing the accelerator size to about a 17 kW power level would meet the 2088 doses per day demand used in the Global '99 study without changing target size or altering the distribution and milking schedule. This is based on the fact that isotope production in an accelerator is directly proportional to beam current, assuming all other factors are constant. Thus doubling power and maintaining electron energy essentially doubles isotope production. It should be noted that an accelerator can be operated at lower beam energies without changing the electron energy, thus allowing a larger accelerator to vary production up to its design limits in beam power.[9]

E. Summary of ^{99}Mo Throughput Options

The ^{99}Mo throughput options from the Global '99 study are summarized in Table 5. The prior melt-technology baseline uses only 5 goats and ends bombardment at 2 a.m. to meet the first milking at 8 a.m. It produces 1376 doses. Next, the inherent efficiency of the corresponding powder-technology baseline improves throughput to yield 1720 doses. The third option doubles the target size to yield the required 2088 doses for Florida—but the distribution of ^{99m}Tc doses to the entire state is impractical from a single, centralized pharmacy. Next, the options for distribution of solid or liquid ^{99}Mo are summarized. For a 7 pharmacy, 35 goat system operating on the schedule to meet airline flights outlined above, a slight increase is needed in ^{99}Mo throughput: 32.3 Ci, up only 1.6% from 31.8 Ci in the centralized pharmacy scenario. While the size of this increase seems surprisingly small, it is a consequence of the somewhat unfavorable schedule adopted in the initial cost estimate study's[2] baseline versus that of the distributed baseline study from Global '99. Note that the throughput increase needed to distribute liquid $(NH_4)_2{}^{99}MoO_4$ is also very modest: 32.9 Ci, up only 1.9% from 32.3 Ci in the solid distribution case. This increase seems quite acceptable given the great flexibility of dispensing and distributing liquid. Finally, an additional option for a 10 day milking schedule is developed for both the solid and liquid cases. A 10 day milking schedule requires 10 goats per pharmacy for a total of 70 goats in the system. However, it had the advantage in 1999 of yielding the entire supply for Florida with no increase in the target size. This is due to the well-known fact that cows (and in this case, goats) can be effectively milked for upwards of two weeks before depleting their ^{99}Mo charge. Finally, as noted in this update, the accelerator could be changed to meet required throughput.

Table 5. Production Throughput Options for ^{99}Mo Distribution in Florida.

Case	Goats	EOB	Mo-99 (Ci)	Doses per Day
Melt Baseline	5	2 a.m.	26.2	1376
Powder Baseline	5	2 a.m.	26.2	1720
Florida-scale baseline	5	2 a.m.	31.8	2088
Distributed (solid†)	35	6 p.m.	32.3	2088
"	70	6 p.m.	25.1	2088
Distributed (liquid††)	35	3 p.m.	32.9	2088
"	70	3 p.m.	25.7	2088

† *Distributed a solid Mo metal target material.*

†† *Distributed as* 2 M $(NH_4)_2MoO_4$ *(aq) aliquots.*

While the 70 goat option seems promising, the 35 goat option with liquid distribution was selected in 1999 as the preferred system baseline for reasons that are described in the next section.

V. IMPACT OF DISTRIBUTED DELIVERY ON THE BASELINE GOAT DESIGN

The initial cost estimate study[2] was baselined on a melt-technology goat, although additional separation experiments were performed with ammonia and nitric-acid-generated powders. These powder milking experiments were performed in both the melt technology goat, and a much smaller provisional unit that could fit through the small access hatch of the Radioanalytical Laboratory (RAL) at the Idaho Nuclear Technology and Engineering Center (INTEC). Neither the melt nor provisional powder units were ideally suited to loading and milking powder: The melt goat had a rather long MoO_3 condenser section which is not entirely necessary for powder milking, as well as a Pt boat that was too small to hold the aqueous sample initially loaded into the unit. On the other hand, the provisional powder unit was assembled with a small clamshell furnace which led to a number of compromises in its design, especially for loading aqueous samples and for ^{99m}Tc washout. While a powder-technology goat has been not specifically designed, the remarks in Section V were aimed at guiding a successful design effort for such a goat.

A. Range of Separated Activity

The detailed milking schedule for the 7-pharmacy network was previously evaluated. It included schedules for each goat at each pharmacy. (Again, there is an equivalency between how many days a goat has been milked and the number of the goat in the herd.) The baseline powder technology goat for a distributed system must yield high separation efficiency over a considerable range of throughput. This range includes both the range of

Table 6. Scaling Requirements on Goats for ^{99m}Tc Separation Throughput.

	Goats in System	Daily ^{99}Mo (Ci)	First/Last Separation (each goat)	Largest Separation (mCi)	Smallest Separation (mCi)	Ratio of Largest to Smallest Separation
	5	31.5	9.5	21,450	2,245	9.5
Baseline:	**35**	**32.2**	**8.9**	**4,630**	**130**	**36**
	70	25.1	31	3,610	30†	120

† *A pharmacy would almost certainly avoid this condition.*

activity from beginning to end of life (15 milkings over 5 days), as well as the fourfold range of required activity between the largest pharmacies (located in Orlando and West Palm Beach) and the smallest pharmacies (in Ft. Myers and Pensacola). Table 6 summarizes the overall range of operation. The distributed baseline is the middle row with 35 goats. In this case the largest activity a goat must separate is 4.63 Ci (on the first milking at the largest pharmacy), and the smallest activity is only 130 mCi (on the last milking at the smallest pharmacy). Thus, a powder goat should be able to separate over the range of 5 Ci down to 100 mCi with high efficiency.

The Global '99 authors noted that the ^{99m}Tc activities quoted in Table 6 are at time of separation, so the last milking at a small pharmacy is only yielding three doses of ^{99m}Tc. Such a small milking could be canceled and offset by a small increase in ^{99}Mo production. In fact, the 5 a.m. and 8 a.m. milkings could be omitted on the last two days of the campaign, which would raise the smallest milking up by nearly a factor of two, to 220 mCi/mL. A complementary alternative would be to extend the milking schedule at the larger pharmacies to 7-10 days. With their larger throughput demand, they would not fall to unacceptable separation levels at the end of life of their goats. Their increased capacity with 7-10 goats would considerably reduce the amount of ^{99}Mo sent to the larger pharmacies, and more than offset the amount of additional ^{99}Mo sent to the smaller pharmacies in order to allow them to avoid the unacceptable operating conditions of 4- to 5-day-old goats. From these considerations it was judged that a goat must be able to separate over the range of 5 Ci down to 200 mCi with high efficiency.

B. Activity Concentration and Elution Volume

In addition to the throughput range, a goat must be able to deliver acceptable activity concentration of ^{99m}Tc in the eluate from the washout operation. The industry expectation is that the activity concentration should be above about 100 mCi/mL, and that some more concentrated eluate (upwards of 300 mCi/mL) must be available for labeling a number of newer, more demanding radiopharmaceuticals. Table 7 summarizes the activity concentration range for the various scenarios. These are derived from the throughput values in Table 6 with the assumption that the baseline goat uses 5 mL of isotonic saline to wash the ^{99m}Tc from a goat. Again the distributed baseline is found in the middle rows with 35 goats. The Initial studies claimed an activity concentration always larger than 500 mCi/mL. This was borne out by the top row, which shows a batch activity concentration (i.e., mixed mean output from all goats at a pharmacy) always greater than 790 mCi/mL. The distributed baseline ranged from 580 mCi/mL for the 2 a.m. milking to 175 mCi/mL for the 8 a.m. milking at the largest pharmacies, and from 155 mCi/mL for the 2 a.m. milking down to only 50 mCi/mL for the 8 a.m. milking at the smallest pharmacy. A similar strategy to the above could overcome the unacceptably low activity concentration of the smallest pharmacy: That is, some milkings could be omitted from the schedule for goats in the smallest

Table 7. Scaling Requirements on Goats for ^{99m}Tc Activity Concentration.

	Goats in System	Pharmacy Site	Biggest Batch (mCi)	Activity Concentration (mCi/mL)	Smallest Batch (mCi)	Activity Concentration (mCi/mL)
	5	-	61,070	2,440	19,800	190
Baseline:	**35**	**Largest**	**14,570**	**580**	**4,370**	**175**
	35	**Smallest**	**3,920**	**155**	**1170†**	**50†**
	70	Largest	14,560	290	4,380	90
	70	Smallest	3,910	80	1180†	25†

† *A pharmacy would almost certainly avoid this condition.*

pharmacies in order to raise the low end of the activity concentration range. Alternatively, the required eluate volume for the goats could be reduced through design and experiments. Generally, a goal elution volume should be 2 mL, down from the current 5 mL. This would result in 100 mCi/mL activity concentration at the lowest throughput (200 mCi) for the range derived above. A further alternative would be to design different size goats for the larger and smaller pharmacies.

C. Goat Cycle Time

As the Global '99 study mentioned, one additional aspect of goat design should be addressed in future design work—reducing the time required to cycle the goat through a milking. Powder goats achieve higher separation efficiency by exploiting the segregation of ^{99m}Tc on the surface of crystals formed when evaporating the solution in the goat. However, this requires the dissolution, evaporation and heating steps outlined in Table 8. It is very important to note that the amount of ^{99m}Tc available for separation must be calculated at the point when the solution finally evaporates: This is near the end of Step 2 in the Unit Operations of the table. Following this, an additional 60-70 minutes are required to complete Steps 3-5 before this ^{99m}Tc is actually available to the radiopharmacist. This implies an 11% reduction in ^{99m}Tc throughput if the one hour wait cannot be accommodated within the average six hour period allotted for labeling, dispensing and distribution before patient administration.

Table 8. Unit Operations to Cycle a Powder Goat.

Unit Operation	Design Cycle Time (min)	Best Possible Cycle Time (min)
1. Add 7 *N* NH_4OH to dissolve residue	20	10
2. Evaporate to dryness without boiling	60	20
3. Heat goat up to milking temperature	30	20
4. Milk ^{99m}Tc at temperature	20	20
5. Cool goat, extract ^{99m}Tc and rinse	20	20
Total Cycle Time	**150** (2 hr 30 min)	**90** (1 hr 30 min)

D. Overall Goat Design Recommendations

The overall Global '99 recommendations for powder goat design are listed in Table 9. In addition to the requirements discussed above, a cost target of $l0K is found in the table. This is necessary to keep the impact on unit cost very low, and is felt to be feasible given the simplicity of the goats. This was increased to approximately $13K for 2007 to account for inflation.

Table 9. Recommended Goat Design Features.

- Loads up to 250 mL aliquot volume for separation
- Unloads boat contents for return to accelerator
- Achieves near-0% sample mass loss per milking cycle
- Achieves high efficiencies: 98% separation, 95% washout
- Separates from 5 Ci (largest) to 200 mCi (smallest) 99mTc
- Achieves 100mCi/mL activity concentration for the smallest separations (2 mL elution volume)
- Total cycle time of 2 hr or less
- Cycle time from precipitation through elute recovery of 1 hr or less
- Cost $5K-10K per goat, including controls and shielding

VI. COMPARISON OF COSTS

A rough cost comparison is summarized in Table 10. The Global '99 baseline study is found in the first column. The overall production cost was 12.8¢ per mCi of ^{99m}Tc at time of administration, some six hours following separation. The present study is found in the second column labeled, '2007 Distributed Separation.' Both assume 35 goats are located at 7 regional nuclear pharmacies. The individual cost components are modified as follows:

- **Facility**- Both facilities have the same design and makeup, but the 2007 cost estimate was adjusted by the construction inflation rates. This was used for obvious costs, such as concrete, gypsum, and steel.[10] The remainder, including design, mechanical equipment, and labor, was adjusted by average inflation.[11]
- **Equipment**- A total of $138K at each of 7 pharmacies was allowed to cover the capital cost of goats and spares (at $13K each) and equipment for washout and recycle of goats. This is adjusted by inflation[11] from the Global '99 $10K cost in 1996.
- **Accelerator**- Identical for both cases. The 2007 cost is inflation adjusted estimate.
- **Target Inventory**- The current price quoted from the DOE Isotope Program Business Office at Oak Ridge National Laboratory (ORNL) is approximately $7500 per gram for calutron-produced 98.6% enriched ^{100}Mo.[12] The authors of the Global '99 baseline study used a cost estimate of $1,000 per gram for ^{100}Mo at 96% enrichment. This difference alone, added 10¢/mCi to the projected price in 2007. The cost of enriched ^{100}Mo will vary by method of enrichment, e.g., centrifuge or calutron, and level of enrichment, e.g., 90% vs. 98.6%, with the latter in each case being the more expensive.[12]
- **Total Capital**- The total capital required is increased by $7.3M by the above considerations.

- **Cost of Capital**- Both cases are based on 20% cost of capital per year.
- **Technician Salaries**- Based on \$53K base salary for technicians plus 50% fringe. The initial study's[2] baseline was reduced by one staff member for the distributed case to reflect not needing to separate ^{99m}Tc at the accelerator. However, one staff member was added at each regional pharmacy to handle goat loading and target material return as well as receipt and shipping of target material.
- **Utilities**- Identical demand for both cases. This cost is dominated by the electric power requirement of the accelerator. Adjusted by the electricity rate increase in Florida from 1996 to 2007 according to Energy Information Agency.
- **Maintenance/Repair**- about \$13K per site per year is added to accommodate goat upkeep adjusted for inflation[11] from the Global '99 estimate of \$10K.
- **Supplies/Services**- This reflects a seven fold increase in cost of ^{100}Mo replenishment, as well as an inflation indexed increase in cost of miscellaneous supplies and services and Klystron refurbishment.
- **Shipping**- This reflects daily air shipments of ^{99}Mo aliquots, plus local ground transportation in the average amount of about \$115 per day per site. This should allow enough contingency within the estimate to handle special shipments and airport cancellations. It is assumed that labor associated with ground transport is covered by the additional technician salary at each site identified above. Both estimates are far above standard freight and would be a fairly conservative estimate.[13]
- **Total Variable**- The total yearly variable cost is increased by about \$2.3M by the considerations above.

Table 10. Updated Distributed vs. Previous Distributed ^{99m}Tc Cost Study Comparison. (Costs in Thousands)

	1996 Distributed Separation		2007 Distributed Separation	
Capital				
Facility	1400 sq. ft.	\$ 910	1400 sq. ft.	\$ 1,258
Laboratory Equipment	Central	345	Central	478
	Local	700	Local	\$969
Accelerator (40 MeV, 14 kW)		2,000		2,768
Target Inventory	900 g	900	900 g	6,633
Total Capital		\$ 4,855		\$ 12,106
Variable				
Cost of Capital		\$ 971		\$ 2,421
Technician Salaries	5 Central	300		403
	7 Local	420		564
Utilities		65	up 9.6%	71
Maintainance/Repair	add \$10K per site	100	add \$13K per site	138
Supplies/Services		300		797
Shipping	\$700/day	218	\$800/day	250
Total Variable		**\$ 2,374**		**\$ 4,645**
Yearly Output		18,613 Ci		18,613 Ci
Unit Cost of 99mTc		**12.8 ¢/mCi**		**25.0 ¢/mCi**

The overall production cost in the 2007 distributed case is approximately doubled to 25.0¢ per mCi of ^{99m}Tc at time of administration, six hours following separation. This increase compares favorably to the market price of ~35¢ per mCi today. Thus, the overall conclusion is that the cost impact of a fully distributed production system in 2007 remains below market pricing of the product.

VII. DISCUSSION

The prior studies developed a cost estimate that included all the costs involved in establishing the facility with all the equipment. In order to update that cost estimate for the purposes of this study, several methods and assumptions were made. The Associated General Contractors of America gave a history of inflation of construction costs. This was used to determine the cost increase for concrete, steel, and gypsum from the Global ‘99 cost estimate. All other costs were increased by inflation of 3% per year. This is approximately the average inflation from 1996 to 2007 and includes a small contingency.[11] Utilities were updated using historical average cost of electricity from 7.99 to 8.76¢ per kilowatt-hour in Florida. Salaries and Equipment were adjusted by 3% inflation. Doubling target size at these costs seems to be the least effective way of achieving the required throughput. The cost of the entire system is heavily based upon the cost of the target material.

If commercial air freight is prohibitive for radioactive materials an alternative method of shipping needs to be available. A second method to estimate shipping of the ^{99}Mo aliquots via a fleet of small company cars was also evaluated. It assumed that the cars had an average of 30 miles to the gallon, and a gallon of gasoline cost $3.03.[14] Also it afforded reasonable delivery times for the pharmacies, because the delivery time would not greatly impact the first milking due to the 1% loss per additional hour stated in the Global ‘99 study. Drivers were to be paid $12.50 an hour and the car payments and insurance were estimated at $200 per month for each vehicle. This still arrives very close to the approximation made above that shipping would average $115 per site per day.

The accelerator and cost of the maintenance for the accelerator was evaluated using a sensitivity study. A $4 Million accelerator using the Global ‘99 methods for payment would only increase the above listed cost by 1.3¢/mCi. A recent estimate offered a much more powerful accelerator with the potential of being in the range this study indicates, but with additional potential for growth, was estimated at about $3.25 million. If this unit were purchased it would increase the cost to produce by only 0.5 ¢/mCi. Additionally the supplies required to maintain the accelerator were estimated at about $40,000 each year, changed from $30,000 in the Global ‘99 study. With $12,000 per year in miscellaneous supplies compared to the initial study’s[2] centralized approximation of $3,000. The replacement of the Molybdenum-100 was also taken into account.

The Global ‘99 study looked at a cost estimate for the whole of Florida, finding that the accelerator model described would supply the demand for Florida. That baseline study was adjusted here to provide options for adjusting the model to any geographic or regional niche for ^{99}Mo production. It was found in the Global ‘99 study based on 1996 cost and population figures that such a system was not only possible, but would be competitive with the then current subsidized reactor base ^{99}Mo production. This study was a look at the process used in the Global ‘99 study, but also addressed 2007 demand in Florida and 2007 cost estimates. The options suggested for increasing throughput would not meet the full demand of Florida. However, it is unlikely that 100% of the market will utilize the goat powder method over the existing cow technology. Therefore, this study included a smaller portion of the Florida market, matched the Global ‘99 study in ^{99m}Tc output, and used current costs for production. Our results show electron accelerator production of ^{99}Mo combined with a distributed regional pharmacy system could be economically feasible in Florida today, and reinforce the findings of the earlier studies that total US demand could be supplied by about 20 such production/distribution systems nationwide.

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